

REMARKS

Pending Claims

Claims 1-7 are pending in the application. No new matter has been added.

Rejection of Claims under 35 U.S.C. § 103(a)

Claims 1, 2 and 4-6 are rejected under 35 U.S.C. §103(a) as obvious in light of U.S. Pat. No. 5,437,982 to Catterall et al. ("Catterall") in view of Connolly et al., Biosensors and Bioelectronics, 1990 5: 223-234 ("Connolly"). In particular, the Examiner states that "[a]t the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have practiced the Catterall invention as discussed above with extracellular electrodes" by combining the teachings of Catterall with Connolly. Office Action of November 17, 2008 at p 4.

However, the Examiner's assertion that Connolly teaches or suggests that extracellular electrodes are a suitable substitute for an intracellular patch clamp (Office Action of November 17, 2008 at page 4) is not accurate. Just because extracellular electrodes can initiate beating of cardiac cells does not mean they are "suitable substitutes" for a patch clamp. The Examiner is referred to Figures 10 and 14 of the application which illustrate examples of the sustained changes made possible with the claimed method. This is qualitatively different from the beating produced by Connolly.

The applicant has stated previously that prior to the present invention, no one thought external electrodes could be used to set transmembrane potential to a desired level so as to manipulate ion channel states. The Examiner has disputed this statement, concluding that Connolly demonstrates that extracellular electrodes were considered substitutes for patch clamping. With this response, the Applicant submits additional evidence that those of skill in the art did not consider using extracellular electrodes as claimed to be obvious.

First, the Examiner's attention is drawn to the attached article "Characterization of voltage-gated sodium-channel blockers by electrical stimulation and fluorescence detection of membrane potential" Nature Biotechnology, Volume 24, Number 4, April 2006. The authors of this article include the inventors of this application. This article, published in a prestigious peer reviewed journal, is directed to demonstrating that it is in fact possible to use extracellular electrodes to reproduce cellular responses previously produced only with patch clamping

techniques. If extracellular stimulation as claimed was obvious based on 1990 work by Connolly, Nature Biotechnology would not publish an article demonstrating the correlation between extracellular stimulation and patch clamping in 2006.

In addition, the Examiner's attention is drawn to U.S. Patent No. 7,276,206 to Augustine et al. ("Augustine"). Relevant pages from Augustine are also attached. This patent, with a priority date about one year later than the present application, begins in its Background section with a discussion of the drawbacks of patch clamping in a high throughput screening environment:

Current methods of drug discovery often involve assessing the biological activity (i.e., screening) of tens or hundreds of thousands of compounds in order to identify a small number of those compounds having a desired activity. In many high throughput screening programs, it is desirable to test as many as 50,000 to 100,000 compounds per day. Unfortunately, current methods of assaying the activity of voltage-gated ion channels are ill suited to the needs of a high throughput screening program. Current methods often rely on electrophysiological techniques. Standard electrophysiological techniques involve "patching" or sealing against the cell membrane with a glass pipette followed by suction on the glass pipette, leading to rupture of the membrane patch (Hamill et al., 1981, Pflugers Arch. 391:85-100). This has limitations and disadvantages. Accessing the cell interior may alter the cell's response properties. The high precision optical apparatuses necessary for micromanipulating the cells and the pipettes make simultaneous recording from more than a few cells at a time impossible. Given these difficulties, the throughput that can be achieved with electrophysiological techniques falls far short of that necessary for high throughput screening.

Next, in column 4, lines 10-20, in the Summary of the Invention section, Augustine states that their inventive solution is using extracellular electrodes to do what had previously been done only with patch clamping:

The present invention is directed to methods of identifying activators and inhibitors of voltage-gated ion channels in which the methods employ electrical field stimulation of the cells via extracellular electrodes in order to manipulate the open/close state transitions of the voltage gated ion channels.

Further, the applicant notes that in column 41 to 48, Augustine copies language of this application as being "embodiments of the subject invention."

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Thus, the publication of the Nature Biotechnology article and the later filed Augustine patent application support the Applicant's assertions that those of skill in the art at the time the invention was made would not find it obvious to manipulate transmembrane potential as claimed with extracellular electrodes.

Thus, for at least the reasons explained above, the limitations recited in Claim 1 would not have been obvious in light of Catterall and Connolly. The remaining prior art of record does not cure the above-mentioned deficiencies with regard to Claim 1. Thus, Applicants respectfully request the Examiner's rejection of independent Claim 1 be reconsidered and withdrawn. Claims 2-7 are dependent on amended Claim 1. It is respectfully submitted that these claims are patentable for at least the same reasons as set forth above with regard to Claim 1.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

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CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the previous Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If any issues remain that could be resolved by telephone, the Examiner is invited to call the undersigned directly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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